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THE COURSE OF EXPERIMENTAL STAPHYLOCOCCUS INFECTION IN ALBINO  
MICE DURING ACTION OF CERTAIN FACTORS OF SPACE FLIGHT

Prokhorov, V. Ya., V. M. Shilov and E. A. Borman

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THE COURSE OF EXPERIMENTAL STAPHYLOCOCCUS INFECTION IN ALBINO MICE  
DURING ACTION OF CERTAIN FACTORS OF SPACE FLIGHT

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One of the current problems of space biology and medicine is to provide for /82\* normal living activity of astronauts in space flight. Recently the literature has provided data evidencing the adverse effect of certain flight factors, in particular acceleration and hypokinesia, on immunological reactivity of the organism (Alekseyeva et al., 1962; Shilov et al., 1966; Mikhaylovskiy et al., 1976). This may lead to lessening of the essential resistance of the macroorganism, the activation of path- /82 ogenic and conditionally pathogenic microflora and the appearance of diseases. Here specific theoretical and practical interest is generated by staphylococcus infection, which plays an important role in the infectious pathology of humans (Vygodchikov, 1963). The wide dissemination of pathogenic staphylococci and their high level of carrier activity among people may lead to the rise of staphylococcal infection for astronauts under prolonged space flight conditions. In this context there is great timeliness in the study of the effect of factors, which are active during space flight, upon the development and outcome of staphylococcal infection. The present report presents the results of a study of the influence of some factors of space flight -- acceleration, hypokinesia and the combined effect of both -- on the course of experimental staphylococcus infection in albino mice.

The experiments were conducted with 200 mongrel male white mice weighing 18-20 g. The animals were divided into 4 groups. Those of group I acted as controls, those of group II were subjected to acceleration overload up to 30 G for 15 minutes, group III were kept under hypokinetic conditions for 30 days and group IV, after spending 30 days in hypokinesia, were subjected to acceleration overload up to 30 G for 15 minutes. This amount of acceleration is possible in space flight emergency situations.

Transverse acceleration was provided by a centrifuge with a 120 cm arm. When the overload was increased to 30 G the general condition of the mice after rotation

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\*Numbers in the margin indicate pagination in the foreign text.

was serious. The overwhelming majority presented signs of orientation loss and paresis of the hindlimbs. By the end of the experiment the mice had lost on the average 1.5-2 g as compared with their initial weight.

Acute staphylococcus infection was induced in the mice by peritoneal administration of a lethal dose ( $10^{9.5}$  living microbial cells in a 0.2 ml volume) of the highly virulent staphylococcus strain L-1726 (phagocyte 80/81). The animals were infected following the action of accelerations, hypokinesia and likewise following the combined effect of accelerations and hypokinesia. At intervals of 15 minutes, 1 hour and 3 hours after infection 3 mice from each group were decapitated each time, their abdominal cavity was opened and a study made of the peritoneal exudate and renal homogenate. The number of live staphylococci was determined by seeding from serial dilutions of the material into dishes with saline agar and then counting colony growth. A study was made of the phagocytic activity of the neutrophils and macrophages in the exudate — phagocyte index and phagocyte count, degree of completeness of phagocytosis (Berman and Slavskaya, 1958). There was a study of the change in content of alpha toxin in the peritoneal exudate and renal homogenate. The method of investigation has been given in greater detail in previous reports (Akatov and Prokhorov, 1968).

The experiments showed, that intraperitoneal infection with a highly virulent strain induced severe staphylococcus infection in all the animals. However the response reaction of the organism was not the same for mice in various groups. Among those of the control group death occurred 5 or 6 hours after infection and included in all 10% of the overall number of mice used in the experiment. For group II death began 4-5 hours following infection and involved 48%. In groups III and IV the highest mortality was observed during earlier periods and already 3-3.5 hours after infection 60% of the animals in these groups had died and after 6 hours all animals had died presenting symptoms of marked intoxication.

The dynamic indices of seedability for staphylococci from the abdominal cavity of mice (Fig. 1) were evidence of the fact, that, in the case of the mice of the control group and group II, who had been subjected to acceleration following the original drop in the microbe count (after 15 minutes), their number gradually grew and continued to do so up to the moment the animals died. Already 15 minutes after infection the microbe count diminished in the experimental animals that were in hypoki-

neria (group III) and those subjected to the combined action of hypokinesia and acceleration (group IV).

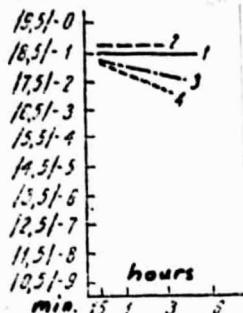


Fig. 1. Seedability of staphylococci from abdominal cavity of mice. Abscissa: 1 g of the number of live coccii; ordinate: time period after infection. 1 - control; 2 - overload; 3 - acceleration; 4 - complex of factors

We know, that a decrease in the number of microbes that can be seeded from the abdominal cavity of mice is a function not only of the destruction of the microorganisms but also of the formation of large microbial aggregates with the interplay of the flocculation factor of the staphylococci and the fibrinogen of the peritoneal exudate from the mice (Kapral, 1965, 1966). Staphylococci in the center of the aggregates are not accessible to phagocytosis; they multiply intensively and exhibit their toxic properties. In our study the most intensive formation of microbial aggregates in the peritoneal exudate was observed in the mice of groups III and IV who had been subjected to hypokinesia and the combined action (Fig. 2) [sic!]. Apparently this also explains the drop in staphylococcus count in the abdominal cavity for animals in the groups referred to. A study of the kidneys (Fig. 3) showed gra-85 dual increase in the number of staphylococci continuing to the moment of animal death. Here the observation was more pronounced seedability of microbes in the kidneys of animals in the test groups, particularly those who had been under hypokinesia and the combined effect.

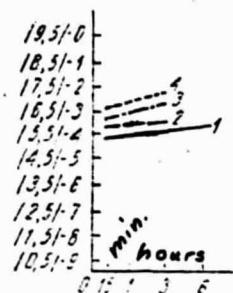


Fig. 3. Seedability of staphylococci from kidneys of mice. Designations as in Fig. 1

A study of the phagocytic activity of the leukocytes (see Table) during the periods closely following infection (after 15 minutes) showed intensive staphylococcus phagocytosis for both test animals and control animals (high phagocyte index and phagocyte count). However in the further course of staphylococcus infection in the test mice there was a concurrent pronounced repression of the leukocytes phagocytic activity. Three hours after infection the phagocyte index and phagocyte count in test mice was significantly lower than for the control. One noticed a large number of disintegrated phagocytes and along with them scattered accumulations of microbes. This pointed to the incompleteness of phagocytosis. Actually, a study of the smears taken after cultivation showed, that from the 15 minute point following infection to

TABLE. PHAGOCYTE ACTIVITY OF LEUKOCYTES IN TEST AND CONTROL ANIMALS

a Группы животных	b Фагоцитарный показатель (в %)			c Фагоцитарное число		
	d срок после заражения					
	15 мин.	1 час	3 часа	15 мин.	1 час	3 часа
Контрольные . . . . .	g	99	94	93	64	53
Заряженные после воздействия перегрузок . . . . .	h	84	61	35	23.2	5.5
Заряженные после пребывания в условиях гипокинезии . . . . .	i	100	78	61	33.4	14.1
Заряженные после комбинированного воздействия . . . . .	j	93	52	35	18.1	2.5

Key: a. Group of animals      e. Minutes  
 b. Phagocyte index (in %)      f. Hour(s)  
 c. Phagocyte count      g. Controls  
 d. Time period following      h. Infected after action of overload  
 infection      i. Infected after period of hypokinesia  
 j. Infected after combined influences

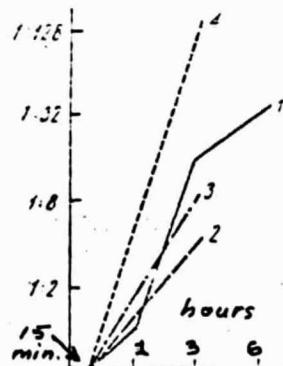


Fig. 4. Dynamics of alpha toxin accumulation in peritoneal exudate of mice.  
 Abscissa: titer of toxin; ordinate: time after infection.  
 Designations as in Fig. 1

This is borne out by the development of a more serious kind of illness along with severe repression of phagocytic activity of the leukocytes and production by the staphylococci of a considerable amount of toxin, which led to quick death for the animals.

the moment of animal death the leukocytes contained only live staphylococci. In the animals of the control group who survived there appeared already after 3 hours a tendency to completion of phagocytosis. Phagocytic activity of the macrophages was more pronounced than that of the neutrophils. Titration of alpha toxin in the peritoneal exudate (Fig. 4) showed that the amount was greatest in the animals subjected to the combined effect (titer 1:128 and higher). No alpha toxin was found in the kidney homogenate.

Thus, the research showed, that acceleration and hypokinesia aggravated the course of staphylococcus infection. The most adverse effect on the course and outcome of the illness was shown by the combined action, which had led to pronounced disruption of the functions of the organism.

### Conclusions

1. Fifteen minutes acceleration with an overload of 30 G and hypokinesia had an adverse effect on the organism and aggravated the course of experimental staphylococcus infection in mice.
2. The most adverse effect on the course and outcome of staphylococcus illness came from the combined effect of hypokinesia and acceleration: the animals showed pronounced depression of phagocytic activity and the formation of a considerable amount of alpha toxin, which caused their rapid demise.

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